# AMENDMENTS TO THE CLAIMS

# 1. (Previously Presented) Pyrimidine derivatives represented by the following formula (I)

in which

ring A stands for a carbocyclic group or heterocyclic group,

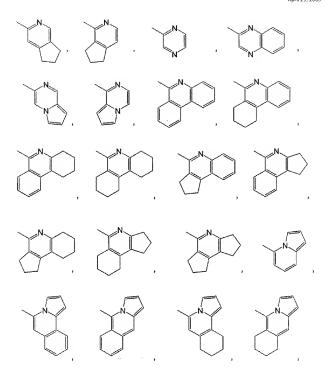
X<sup>1</sup> stands for amino, lower alkylamino, di-lower alkylamino, lower alkylideneamino, lower alkyl, phenyl lower alkyl or substituted or unsubstituted phenyl,

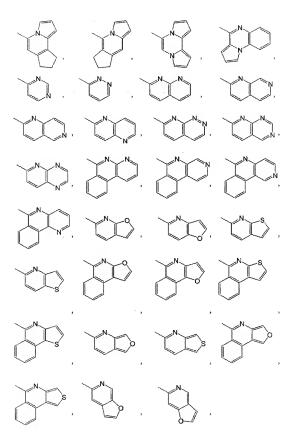
X2 stands for hydrogen or lower alkyl,

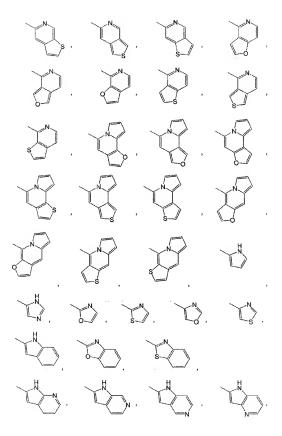
Y stands for a direct bond, sulfur or nitrogen,

n is 0 or an integer of 1 - 4,

Ar stands for a group represented by any of the following formulae,







which are, independently from each other, either unsubstituted or substituted with substituent(s) selected from halogen, lower alkyl, hydroxyl, lower alkoxy and phenyl, or their pharmaceutically acceptable salts.

2. (Original) The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1, in which the ring A stands for a carbocyclic group represented by any of the following formulae i) – iv):

in which

R<sup>1</sup> stands for hydrogen, halogen, lower alkyl, halogenated lower alkyl, lower alkoxy, carboxyl, lower alkoxycarbonyl, phenyl, amino, hydrazino or nitro.

 $R^2$ ,  $R^3$  and  $R^4$  either stand for, independently from each other, hydrogen, halogen, lower alkyl, lower alkoxy, phenyl or hydroxyl; or two out of  $R^2$ ,  $R^3$  and  $R^4$  together stand for oxo or lower alkylenedioxy, and

m is an integer of 1 - 3.

- (Original) The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 2, in which the ring A stands for a carbocyclic group represented by the formula ii).
- 4. (Original) The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 3, in which m is 2.

- 5. (Original) The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 4, in which all of  $\mathbb{R}^2$ ,  $\mathbb{R}^3$  and  $\mathbb{R}^4$  stand for hydrogen atoms.
- 6. (Original) The pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1, in which the ring A stands for a heterocyclic group represented by any of the following formulae v) xv):

in which

R<sup>5</sup> stands for hydrogen, lower alkyl, carboxyl or lower alkoxycarbonyl,

R6 stands for hydrogen or lower alkyl.

and

 $R^7$  stands for hydrogen, lower alkyl, lower alkanoyl, lower alkoxycarbonyl or phenyl lower alkoxycarbonyl.

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7. (Cancelled)

8. (Previously Presented) The pyrimidine derivatives or their pharmaceutically acceptable salts

as set forth in Claim 1, in which X1 stands for amino or lower alkyl.

9. (Previously Presented) The pyrimidine derivatives or their pharmaceutically acceptable salts

as set forth in Claim 1, in which X2 stands for hydrogen.

10. (Previously Presented) The pyrimidine derivatives or their pharmaceutically acceptable salts

as set forth in Claim 1, in which Y stands for a direct bond or sulfur.

11. (Previously Presented) The pyrimidine derivatives or their pharmaceutically acceptable salts

as set forth in Claim 1, in which n stands for 2 or 3.

12. (Previously Presented) The pyrimidine derivatives or their pharmaceutically acceptable salts

as set forth in Claim 1, in which Ar stands for quinolyl group which is either unsubstituted or

 $substituted\ with\ substituent (s)\ selected\ from\ halogen,\ lower\ alkyl,\ hydroxyl,\ lower\ alkoxy\ and$ 

phenyl.

13. (Previously Presented) A pyrimidine derivative selected from the group consisting of the

following compounds or pharmaceutically acceptable salt thereof:

3-amino-5,6-dimethyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-3H-thieno[2,3-d]pyrimidin-

4-one,

3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8- tetrahydro-3H-

benzo[4,5]thieno[2,3-d]pyrimidin-4-one,

3-amino-5,6-dimethyl-2-[3-(4-pyrrolo[1,2-a]quinoxalin-4-ylpiperazin-1-yl)propylthio]-3H-

thieno[2,3-d]pyrimidin-4-one,

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3-amino-5-methyl-4-oxo-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]- 3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid ethyl ester,

3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8,9,10- hexahydro-3H-11-thia-1,3-diazacveloocta[a]inden-4-one.

3-amino-7-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]- 5,6,7,8-tetrahydro-3Hbenzo[4.5]thieno[2.3-d]pyrimidin-4-one.

3-amino-2-[3-[4-(4-methylquinolin-2-yl)piperazin-1-yl]propylthio]- 5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one,

3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8- tetrahydro-3H-9-thia-1,3,7-triazafluoren-4-one.

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4- one,

3-amino-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-3H- quinazolin-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- thieno[3,2-d]pyrimidin-4-one,

3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- quinazolin-4-one,

3-amino-2-[4-[4-(5-methoxyquinolin-2-yl)piperazin-1-yl]butyl]-3H- quinazolin-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- thieno[2,3-d]pyrimidin-4-one,

3-amino-5-chloro-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- quinazolin-4-one,

3-amino-5-hydrazino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- quinazolin-4-one,

3-amino-5,6-dimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- thieno[2,3-d]pyrimidin-4-one,

3-amino-8-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one.

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3,5,6,7,8,9- hexahydrocvcloheptald[pvrimidin-4-one,

3-amino-6-fluoro-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- quinazolin-4-one,

3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one,

3-amino-6-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one,

3-amino-6-hydroxy-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one.

3-amino-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamine]-5,6,7,8- tetrahydro-3H-quinazolin-4-one.

3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro- 3H-quinazolin-4-one,

3-methyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one.

3-ethyl-2-[4-[4-(4-methylquinolin-2-yl])piperazin-1-yl]butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one

3-benzyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8- tetrahydro-3H-quinazolin-4-one.

3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4- one,

3-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4- one,

6-chloro-3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H- quinazolin-4-one.

3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-5,6,7,8- tetrahydro-3H-quinazolin-4-one, and

3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylthio]-3H- quinazolin-4-one.

14. (Previously Presented) Serotonin receptor subtype 3 (5-HT<sub>3</sub>) antagonistic agents concurrently having serotonin receptor subtype 1A (5-HT<sub>1A</sub>) agonistic activity, said agents containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1

15. (Previously Presented) Medical compositions containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in Claim 1 and pharmaceutically acceptable carriers. 16. (Previously Presented) Treating agents for irritable bowel syndrome (IBS) containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in claim 1.

#### 17. (Cancelled)

18. (Currently Amended) The method as set forth in Claim 17, in which the 5-HT, antagonistic-agent concurrently having 5-HT<sub>1A</sub> agonistic activity is a pyrimidine derivative or a pharmaceutically acceptable salt thereof as set forth in Claim 1.—

A method for treating irritable bowel syndrome (IBS) by exerting 5-HT<sub>1A</sub> agonistic activity and 5-HT<sub>3</sub> antagonistic activity *in vivo* simultaneously and cooperatively, which comprises

administering to a human being or other mammals who requires irritable bowel syndrome
(IBS) therapy, a 5-HT<sub>3</sub> antagonistic agent which concurrently exhibits 5-HT<sub>1A</sub> agonistic activity.

in which the 5-HT<sub>3</sub> antagonistic agent which concurrently exhibits 5-HT<sub>1A</sub> agonistic activity is a pyrimidine derivative selected from the group consisting of the following compounds, or their pharmaceutically acceptable salt:

 $\label{lem:conditional} 3-amino-5, 6-dimethyl-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]-3H-thieno[2,3-d]pyrimidin-4-one.$ 

3-amino-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]-5,6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one.

3-amino-5,6-dimethyl-2-[3-(4-pyrrolo[1,2-a]quinoxalin-4-ylpiperazin-1-ylpropylthio]-3H-thieno[2,3-d]pyrimidin-4-one,

3-amino-5-methyl-4-oxo-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid ethyl ester,

3-amino-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]-5.6,7,8,9,10- hexallydro-3H-11-thia-1,3-diazacycloocta[a]inden-4-one.

3-amino-7-methyl-2- [3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]- 5.6,7,8-tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one,

3-amino-2-[3-[4-(4-methylquinolin-2-yl)piperazin-l-yl]propylthio]-5.6,7.8-

tetrahydro-3H-benzo[4,5]thieno[2,3-d]pyrimidin-4-one.

3-amino-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylthio]-5,6,7,8- tetrahydro-3H-9-thia-1,3, 7-triazafluoren-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin -l-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one.

3-amino-2-[4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-3H-quinazolin-4-one.

3-amino-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-3H-quinazolin-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[3,2-d]pyrimidin-4-one,

3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-3H-quinazolin-4-one,

3-amino-2-[4-[4-(5-methoxyquinolin-2-yl)piperazin-l-yl]butyl]-3H-quinazolin-

4-one,

3-amino-2-[4-(4-quinolin -2-ylpiperazin-l-yl)butyl]-3Hthieno[2,3-d]pyrimidin-4-one,

 ${\color{blue}3-amino-5-chloro-2-[4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-3H-quinazolin-4-one.}$ 

 $3\text{-}amino-5\text{-}hydrazino-2\text{-}[4\text{-}(4\text{-}quinolin-2\text{-}ylpíperazin-1\text{-}yl)butyl]}\text{-}3Hquinazolin-4\text{-}one.$ 

3-amino-5,6-dimethyl-2-[4-(4-quinolin-2-ylpiperazin -l-yl)butyl]-3H-thieno[2,3-d]pyrimidin-4-one,

3-amino-8-methyl-2-[4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-amino-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3,5,6,7,8,9- hexahydro-cyclohepta[d]pyrimidin-4-one,

3-amino-6-fluoro-2-[4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-3H-quinazolin-4-one,

3-amino-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-amino-6-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one.

3-amino-6-hydroxy-2-]4-(4-quinolin-2-ylpiperazin-l-yl)butyl]-5,6,7,8- tetrahydro-3H-

quinazolin-4-one,

3-amino-2-[3-(4-quinolin-2-ylpiperazin-l-yl)propylamine]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H -quinazolin-4-one.

3-methyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one.

3-ethyl-2-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-benzyl-2-[4-[4-(4-methylquinolin-2-yl)piperazin-1-yl]butyl]-5,6,7,8-tetrahydro-3H -quinazolin-4-one,

3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

3-ethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

6-chloro, -3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one.

3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1yl)propylthio]-5,6,7,8-tetrahydro-3H-quinazolin-4-one.

 $\underline{3\text{-methyl-2-[3-(4-quinolin-2-ylpiperazin-1yl)propylthio]-3H-quinazolin-4-}}$ 

one,

3-benzyl-2-[4-(4-quinolin -2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H - quinazolin-4-one,

3-methyl-2-[3-(4-quinolin -2-ylpiperazin-1-yl)propyl]-5,6,7,8-tetrahydro-3H - quinazolin-4-one.

2-[4-(4-benzothiazol-2-ylpiperazin-1-yl)butyl]-3-methyl-5,6,7,8-

tetrahydro-3H-quinazolin-4-one.

2-[4-(4-benzothiazol-2-ylpiperazin-1-yl)butyl]-3-ethyl-5,6,7,8-tetrahydro-3H -quinazolin-4-one,

2-[4-(4-benzothiazol-2-ylpiperazin-1-yl)butyl]-3-benzyl-5,6,7,8-tetrahydro-3H -quinazolin-4-one.

3,6-dimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one.

3-ethyl-6-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-5.6.7,8-tetrahydro-3H-quinazolin-4-one,

3-methyl-2-[4-)4-quinolin-2-ylpiperazin-1-yl)pentyl]-5,6,7,8-tetrahydro-3H-quinazolin-4-one,

3-isopropyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

3-benzyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

3-(4-methoxyphenyl)-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one

5-chloro-3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-

### quinazolin-4-one.

1.5-dimethyl-6-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-1,5-

dihydropyrazolo[3,4-d]pyrimidin-4-one,

6,7-dimethoxy-3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

3,5,6-trimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-thieno[2,3-dlpyrimidin-4-one.

3.7-dimethyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one,

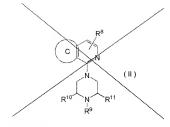
6-bromo-3-methyl-2-[4-(4-quinolin-2-ylpiperazin-1-yl)butyl]-3H-quinazolin-4-one.

3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamino]-5,6,7,8-tetrahydro-

3H-quinazolin-4-one, and

3-methyl-2-[3-(4-quinolin-2-ylpiperazin-1-yl)propylamine]-3H-quinazolin-4-one.

19. (Currently Amended) The method as set-forth in Claim 17, in which the 5-HT<sub>3</sub> antagonistic agents concurrently having 5-HT<sub>1A</sub> agonistic activity are piperazinylpyridine derivatives represented by the following formula (II);



in which

ring C stands for unsubstituted benzene ring or an unsubstituted heterocyclic groupselected from pyridine, furan and thiophene, benzene ring substituted with substituent(s) selectedfrom halogen, lower-alkyl, phenyl, hydroxyl, lower-alkoxy, phenyl-lower-alkoxy (the phenylmoiety being either unsubstituted or halogen-substituted), amino, lower-alkylamino, di-loweralkylamino, lower-alkylthio, lower-alkylsulfinyl and aminosulfonyloxy, or heterocyclic groupselected from halogen- or lower alkyl-substituted pyridine, furan and thiophene,

R<sup>8</sup>-stands for hydrogen, halogen or lower alkyl,

R<sup>o</sup> stands for hydrogen, lower alkyl, phonyl lower alkyl (the phenyl moiety beingunsubstituted or substituted with substituent(s) selected from halogen, lower alkyl and loweralkoxy), amino lower alkyl (the amino-moiety-being either unsubstituted or mono- or disubstituted with lower alkyl, or optionally forming a cyclic imido group) or phenyl cycloalkyl (the phenyl moiety-being either unsubstituted or substituted with substituent(s) selected from halogenlower alkyl and lower alkoxyl.

R40 stands for hydrogen or lower alkyl, or

R<sup>o</sup> and R<sup>10</sup> may together form the residual members of pyrrolidine ring or piperidine ring-(which may be unsubstituted or substituted with substituent(s) selected from hydroxyl, loweralkoxy and phenyl-lower-alkoxyl, and-

R<sup>11</sup> stands for hydrogen or lower alkyl, or their pharmaceutically acceptable salts...

Michitaka SATO et al. Serial No. 10/590,707 Attorney Docket No. 2006\_1414A April 29, 2009

A method for treating irritable bowel syndrome (IBS) by exerting 5-HT<sub>1A</sub> agonistic activity and 5-HT<sub>2</sub> antagonistic activity in vivo simultaneously and cooperatively, which comprises administering to a human being or other mammals-who requires irritable bowel syndrome.

(IBS) therapy, a 5-HT<sub>2</sub> antagonistic agent which concurrently exhibits 5-HT<sub>1A</sub> agonistic activity, in which the 5-HT<sub>1A</sub> is a

piperazinylpyridine derivative selected from the group consisting of the following compounds, or their pharmaceutically acceptable salt:

7-chloro-1-(4-methylpiperazin-1-yl)isoquinoline,

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)thieno[2,3-c]- pyridine.

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)furo[2,3-c]- pyridine.

2-methyl-4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)- thieno[3,2-c]pyridine.

7-methoxy-1-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)- isoquinoline,

2-bromo-4-(4-methylpiperazin-1-vl)thienof3,2-clpyridine.

7-piperazin-1-ylfuro[2,3-c]pyridine.

4-(4-methylpiperazin-l-yl)furo[2,3-c]pyridine,

7-(4-methylpiperazin-l-yl)thieno[2,3-c]pyridine,

4-(4-methylpiperazin-l-yl)thieno[3,2-c]pyridine,

 ${\it 3-chloro-l-} (4-methylpiperazin-l-yl) is oquinoline\ dihydrochloride,$ 

7-(4-ethylpiperazin-l-yl)-thieno[2,3-c]pyridine,

8-(4-methylpiperazin-1-yl)[1,7]naphthyridine,

2-methylpiperazin-l-ylfuro[3,2-c]pyridine,

7-methoxy-4-methyl-1-piperazin-1-ylisoquinoline,

7-bromo-l-piperazin-l-ylisoquinoline,

7-methoxy-l-(4-methylpiperazin-l-yl)isoquinoline,

7-methoxy-1-piperazin-1-ylisoquinoline.

1-piperazin-l-ylisoquinoline,

7-methoxy-1-(3-methylpiperazin-1-yl)isoquinoline.

6-methoxy-l-piperazin-l-ylisoquinoline,

7-methyl-l-piperazin-l-ylisoquinoline,

7-methyl-l-(4-methylpiperazin-l-yl)isoquinoline,

7-chloro-l-piperazin-l-ylisoquinoline.

7-fluoro-l-(4-methylpiperazin-l-yl)isoquinoline,

6-chloro-l-piperazin-l-ylisoquinoline,

5-chloro-l-(4-methylpiperazin-l-yl)isoquinoline,

7-fluoro-1-piperazin I-ylisoquinoline,

1-(4-benzo[1,3]dioxol-5-vlmethylpiperazin-l-yl)-7-methoxyisoquinoline.

1-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)-7-methoxyisoquinoline,

7-chloro-l-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)isoquinoline.

8-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)-1,7-naphthyridine,

7-chloro-l-((8aR)-octahydlropyrrolo[1,2-a]pyrazin-2-yl)isoquinoline,

7-methoxy-l-octahydropyrido[1,2-a]pyrazin-2-ylisoquinoline,

7-methylsulfanyl-I-(S)-octahydropyrido[1,2-a]pyrazin-2-ylisoquinoline,

1-(S)-octahydropyrido[1,2-a]pyran-2-yl-7-hydroxyisoquinoline,

I-(S)- octahydropyrido[1,2-a]pyran-2-yl-7-sulfamoylisoguinoline,

7-dimethylamino-l-(4-methylpiperazin-l-yl)isoquinoline.

7-hydroxy-1-piperazin-1-ylisoquinoline hydrochloride,

7-(4-fluorobenzyloxy)-1-piperazin-l-ylisoquinoline,

4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-y1)thieno[3,2-c]pyridine,

4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)furo[3,2-c]pyridine,

2-bromo-4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)thieno[3,2-c]-pyridine.

7-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)thieno[2,3-c]pyridine,

 $4 \hbox{-} ((8aR) \hbox{-} octahydropyrrolo \hbox{$[1,2-a]$ pyrazin-$2-yl$)} thieno \hbox{$[3,2-c]$ pyridine},$ 

7-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)furo[2,3-c]pyridine,

7-((7R,8aS)-7-hydlroxyoctahydropyrrolo[1,2-a]pyrazin-2-yl)furo[2,3-c]pyridine.

 $7\hbox{-}((7R,8aS)\hbox{-}7\hbox{-}hydroxyoctahydropyrrolo} \hbox{\small [1,2-a]} pyrazin-2\hbox{-}yl) thieno} \hbox{\small [2,3-a]} pyrazin$ 

# clpyridine.

4-((8aR)-octahydropyrrolof 1,2-a]pyrazin-2-yl)furo[3,2-c]pyridine,

4-((7R,8aS)-7-hydroxyoctahydropyrrolo[1,2-a]pyrazin-2-yl)furo[3,2-c]-

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pyridine,

4-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)-2-methylfuro[3,2-c]pyridine.

7-((7R,8aS)-7-benzyloxyoctahydropyrrolo[1,2-a]pyrazin-2-y1)thieno-[2,3-

clpyridine,

4-((7R,8aS)-7-benzyloxyoctahydropyrrolo[1,2-a]pyrazin-2-yl)thieno-[3,2-c]pyridine,

7-octahydropyrido[1,2-a]pyrazin-2-ylfuro[2,3-c]pyridine,

4-octabydropyrido[1,2-a]pyrazin-2-ylfuro[3,2-c]pyridine,

7-octahydropyrido[1,2-a]pyrazin-2-ylthieno[2,3-c]pyridine, and

4-octahydropyrido[1,2-a]pyrazin-2-ylthieno[3,2-c]pyridine.

20. (Currently Amended) The method as set forth in Claim 19, in which the 5-HT<sub>3</sub> antagonistic agents-which concurrently having-exhibits.5-HT<sub>1A</sub> agonistic activity are is a piperazinylpyridine derivatives selected from the group consisting of the following compounds, or their pharmaceutically acceptable salts:

7-chloro-1-(4-methylpiperazin-1-yl)isoquinoline,

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)thieno[2,3-c]- pyridine,

7-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)furo[2,3-c]- pyridine,

2-methyl-4-((8aS)-octahydropyrrolo[1,2-a]pyrazin-2-yl)- thieno[3,2-c]pyridine,

7-methoxy-1-((8aR)-octahydropyrrolo[1,2-a]pyrazin-2-yl)- isoquinoline, and

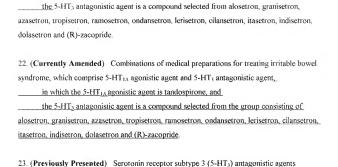
2-bromo-4-(4-methylpiperazin-1-yl)thieno[3,2-c]pyridine.

21. (Currently Amended) The method as set-forth in Claim 17A method for treating irritable bowel syndrome (IBS) by exerting 5-HT<sub>1A</sub> agonistic activity and 5-HT<sub>3</sub> antagonistic activity in vivo simultaneously and cooperatively, which comprises.

administering to a human being or other mammals who requires irritable bowel syndrome (IBS) therapy, a 5-HT<sub>1A</sub> agonistic agent and a 5-HT<sub>3</sub> antagonistic agent simultaneously, or in sequence, or at an interval,

in which the 5-HT<sub>1A</sub> agonistic agent is tandospirone, and

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24. (**Previously Presented**) Medical compositions containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in claim 13 and pharmaceutically acceptable carriers.

concurrently having serotonin receptor subtype IA (5-HT<sub>LA</sub>) agonistic activity, said agents containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in

claim 13.

25. (Previously Presented) Treating agents for irritable bowel syndrome (IBS) containing the pyrimidine derivatives or their pharmaceutically acceptable salts as set forth in claim 13.